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Development of Novel LOVE wave biosensor for simultaneous detection of multi-analyte

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Abstract

In this paper, a novel 208MHz LOVE wave biosensor with one reference element and three sensing elements was developed in a single sensor. PMMA was chosen for the waveguide layer because it can be easily produced using a spin-coating technique. In addition, PMMA has a relatively low density (1.17 g/cm^3), low SH velocity (1105 m/s), a good elastic property, and high stiffness modulus (1.7 GPa). The developed sensor shows high sensitivity, and detects three different biomolecules and improves the reliability of results using reference element. The evaluated sensitivity of the sensor was 7 kHz/ mg^a•ml^{-1}. Long-term stabilities of the developed sensor in liquid environment were also observed. From these results, we confirmed that the developed Love wave biosensor is very promising for simultaneous detections of multi-bioanalyte in a single sensor and for improving the reliabilities of the sensors.

Kewords: Love wave, Multi detection, mass loading sensitivity, PMMA

1. Introduction

Surface Acoustic Wave (SAW) devices have been successfully used for biosensing purposes, exhibiting high sensitivity in mass deposition, viscous and/or viscoelastic changes, as well as in the detection of conformational changes of surface bound biomolecules. Love wave sensors have been employed in liquids for biochemical and chemical applications due to the high sensitivity and possibility of label free detection. Recent advances in biology require the development of platforms that are capable of detecting a large number of analytes leading to multiplexing of the results and better understanding of

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biomolecular interactions. To achieve selectivity, several sensor devices must then be combined into a sensor array. An array of polymer coated surface acoustic wave (SAW) sensors with different sensitive coatings and suitable data processing allows retrieving the qualitative as well as the quantitative composition of the volatiles of interest [1].

2. Operation principle and result

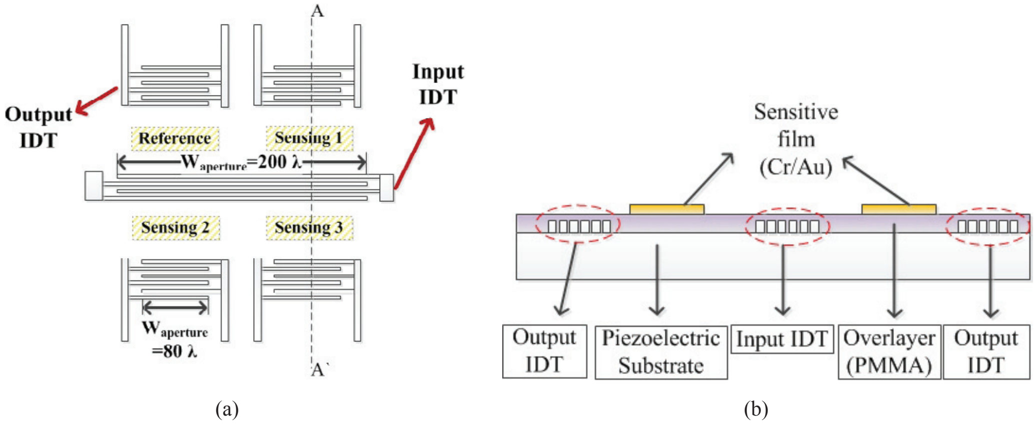


Fig. 1. Schematic views of the developed biosensor (a) Top view of the biosensor (b) Cross-sectional views along A-A`

Figure 1 shows a schematic diagram of the developed biosensor. It consists of one input interdigital transducer (IDT), four sets of output IDTs, an overlayer to generate LOVE wave and four sensitive films. One of output IDTs is used for reference element which compensates any changes originated by environmental factors. Others are used for sensor elements. The binding of different concentrations of IgG to the protein A receptor layer at sensor elements induces a change in mass loading and Love wave velocity, resulting in the frequency shifts of sensor elements. By analyzing frequency shifts of the three sensor elements, we can extract three different IgG concentrations at the same time.

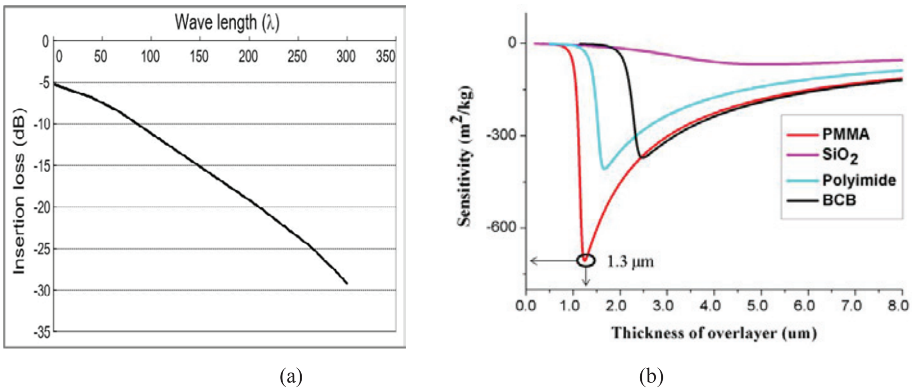
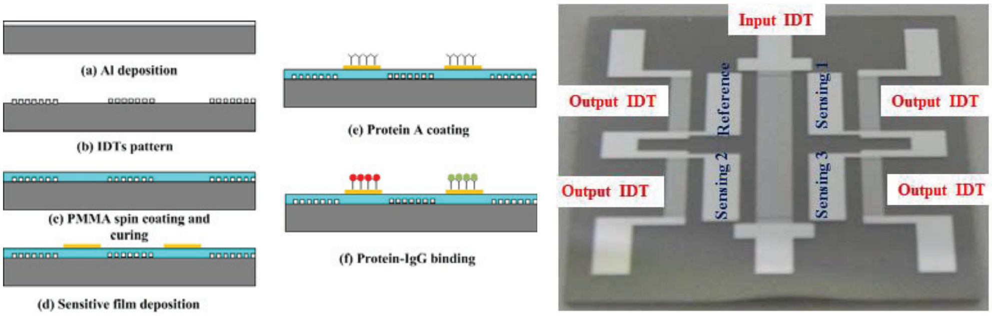


Fig. 2. (a) Simulated insertion loss as a function of input IDT aperture lengths and (b) calculated sensitivity as a function of different overlayer materials and thicknesses.

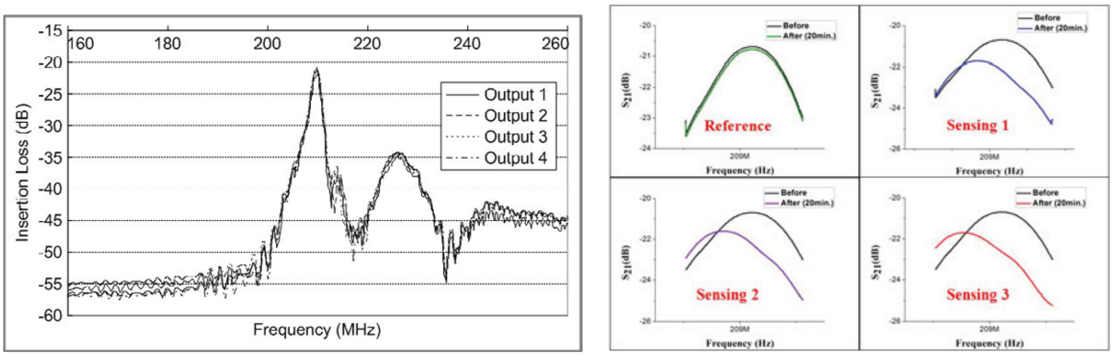
To minimize any deviations of the output IDTs, single input IDT structure employed for this biosensor. Owing to single input IDT structure, the aperture of input IDT has to be longer. To obtain the optimum aperture, the simulation using coupling of mode (COM) was carried out as shown in fig 2(a). Based on the simulation results, optimal aperture length was considered to be 200·λ (wavelength $\lambda = v_{substrate} / f_{operation}$). To minimize the insertion loss and electric feedthrough effect, split electrode IDT was used. The overlayer in the LOVE wave sensor is one of the most important factors, because the generated LOVE wave largely relies on the overlayer characteristics. Of several different overlayer materials, PMMA was chosen for the overlayer material, because it has a relatively low density (1.17 g/cm), low SH velocity (1105 m s^{-1}), good elastic property, and high stiffness modulus (1.7 GPa). To compare the PMMA and other materials, the simulations using the dispersion equation and perturbation theory were carried out as shown in fig 2(b). A 36° YX $LiTaO_3$ was used for the piezoelectric substrate because it provides a leaky SH wave mode with high velocity (4160 m/s), large electromechanical coupling factor (5%), which will be of benefit for the loss mechanism improvement of Love wave device.



(a) *(b)*

Fig. 3. (a) Fabrication procedure and immobilization process and (b) optical view of fabricated device

Figure 3(a) shows the fabrication procedure of a LOVE wave sensor. The device was placed in a sealed container and exposed to PBS buffer (phosphate buffered saline tablets (0.01 M phosphate, 2.7 mM potassium chloride, and 0.137 M sodium chloride, pH 7.4)), which was then shaken at 100 rpm by a shaker for approximately 1 h. Next, protein A was added to the PBS buffer to make a solution of 10 mg/ml protein A. The concentration of the protein A was high enough to saturate absorption sites on the gold surface. It is well known that the protein A concentration in solution influences. Figure 3(b) shows optical view of fabricated devices.

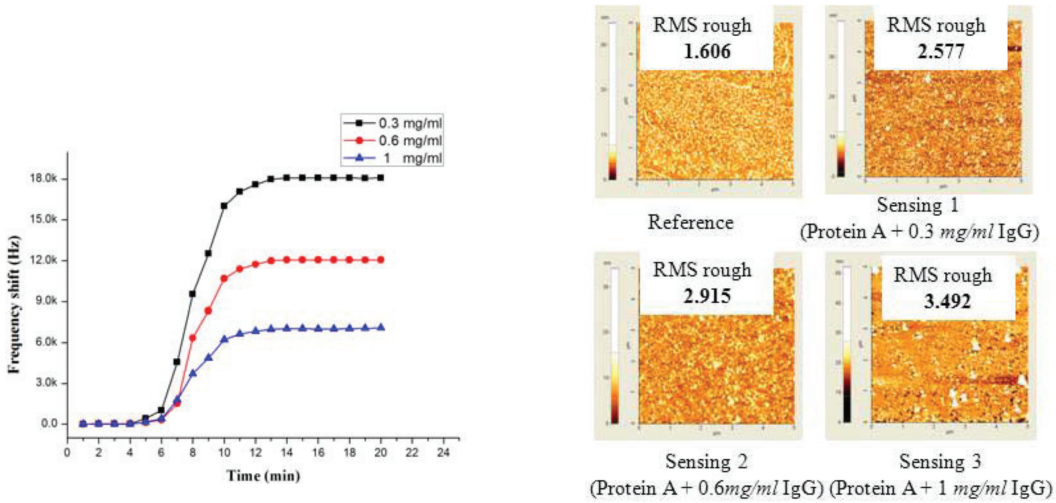


(a) (b)

Fig. 4. Measured S21 of the fabricated devices in air under 25◦C and 50% absolute humidity

Before bio-testing, the fabricated device was characterized by the network analyzer. Signals at respective output IDTs were almost identical as shown in figure 4(a). This result proves that single input

IDT structure is effective. The IgG solutions with different concentrations were dropped onto the sensitive films (Sensor 1→0.3 mg·ml^{-1}, Sensor 2→0.6 mg·ml^{-1}, and Sensing 3→1 mg·ml^{-1}) and then measured the frequency shifts in the network analyzer. Disparate frequency shifts in three sensing elements were observed as shown in figure 4 (b).



(a) (b)

Fig. 5. (a) Frequency shifts as a function of time for different IgG concentrations and (b) AFM image of sensitive film after immobilization

During the measurement, temperature and humidity were constantly remained at 25◦C and 50% absolute humidity. No frequency shifts were observed in the reference element, which means the reference element was not affected by bio material but merely environmental effect. Figure 5(a) shows the frequency shifts of the fabricated sensor (with 1.3μm PMMA thickness and Protein A receptor) as a function of time at respective output IDTs. The frequency shifts increase linearly with increasing IgG concentrations. The evaluated sensitivity of the sensor was 7 kHz/ mg•ml^{-1}. Long-term stabilities of the developed sensor in liquid environment were also observed. To evaluate the surface topography of the sensitive film, AFM measurement was performed after the immobilization as shown in Fig. 5(b). RMS roughs of sensitive films were 1.606(reference), 2.577(sensing 1), 2.915(sensing 2) and 3.492(sensing 3).

3. Conclusion

In this paper, a novel 208MHz LOVE wave biosensor with one reference element and three sensing elements was developed in a single sensor. The evaluated sensitivity of the sensor was 7 kHz/ mg•ml^{-1}. Long-term stabilities of the developed sensor in liquid environment were also observed. From these results, we confirmed that the developed Love wave biosensor is very promising for simultaneous detections of multi-bioanalyte in a single sensor and for improving the reliabilities of the sensors.

References

[1] Kovacs G, Vellekoop M J and Hauels R 1994 Love waves for (bio) chemical sensing in liquids Sensors Actuators A 43 38–43.